Thesis Summary

Photochemical [2+2] Cycloaddition Reaction of Carbonyl Compounds with Danishefsky-Kitahara Diene
(Danishefsky-Kitahara ジエンとカルボニル化合物との光[2+2]付加環化反応)

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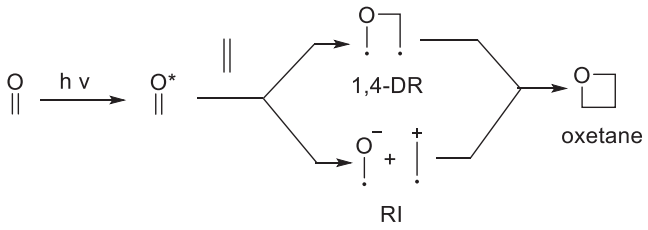
Photochemical reactions occur all around us, being an essential aspect of many of the chemical processes occurring in living systems and in the environment. The capability and versatility of photochemistry are increasingly becoming important in improving the quality of our lives through health care, energy production, and the search for solutions to some of the problems of the modernized world. Many industrial and technological processes depend on applications of photochemistry. The development of many new devices has been made possible by the result of photochemical research.[1]

When a molecule absorbs light, it can reach an electronically excited state. As a result, the distribution of electrons in the molecule is significantly different from that in the ground state. The chemical property and reactivity of the excited state also change. The photochemical reactions may substantially shorten the number of steps in organic synthesis. The complex, polycyclic, or highly functionalized structures can be obtained from simple substrates. New products that are challenging in synthesis using ground-state reactions are thus available, opening new perspectives in search of biologically active compounds.[2]

The photochemical [2+2] cycloaddition reaction of alkenes with carbonyl compounds, referred to as the Paternò–Büchi (PB) reaction, was first reported in 1909[3,4] and is currently one of the versatile methods for oxetane synthesis (Scheme 1). Recent interest in this heterocycle is partly due to its biological activity. Oxetane rings have gained significant attention in medicinal chemistry as they can replace the gem-dimethyl and carbonyl groups to increase the "druglike" properties of a compound, especially its water solubility.[5] Several biologically active oxetane-containing compounds have been found in nature, including 7-epi-10-deacetyltaxol with anticancer activity,[6] norfriedelin A with acetylcholinesterase inhibitor activity,[7] and macrolactins with antimicrobial activity.[8]

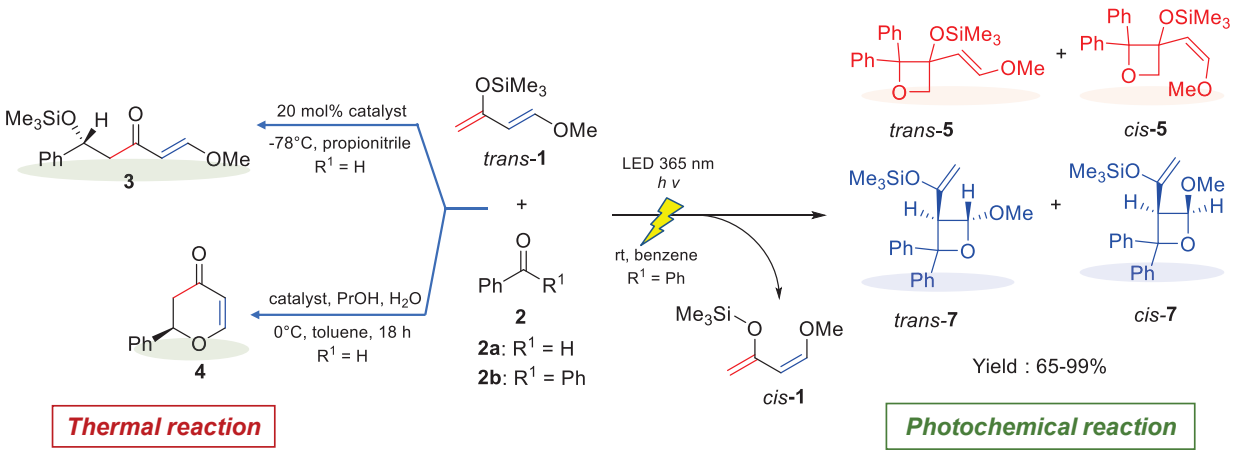


Scheme 1 General mechanism of Paternò–Büchi reaction

Danishefsky and Kitahara developed an acyclic siloxydiene, *trans*-1-methoxy-3-trimethylsilyloxy-buta-1,3-diene (*trans*-**1**). It is also known as the Danishefsky diene and is an useful reagent in organic synthesis.[9] Since the diene is an electron-rich nucleophile, it proved to be a powerful reagent in the Mukaiyama aldol addition and Diels-Alder reactions. For example, the reaction of benzaldehyde (**2a**) with *trans*-**1** at

−78 °C in propionitrile solvent in the presence of 20 mol% acid catalyst afforded mainly the Mukaiyama aldol product **3** (Scheme 2).[10] The C1 carbon of *trans*-**1** is the most nucleophilic centre, and thus, reacts with the electrophilic carbonyl carbon of **2a** to give the final 1,3 ketol product **3**. The hetero Diels-Alder reaction of **2a** with *trans*-**1** using a chiral zirconium catalyst[11] gave the pyranone product **4** in 35% yield and 62% ee selectivity (Scheme 2).[12]

In this study, the PB reaction of *trans*-**1** with benzophenone (**2b**) was examined for the first time, in which the formation of oxetanes **5** and **7** were found in high yields.[13] So far, the PB reaction of acyclic conjugated dienes has not been studied. This is because the dienes are well-known to physically, rather than chemically, quench the triplet state of ketones, owing to their low triplet energy, E_T (~ 55 kcal mol^{-1}). The photochemically activated carbonyl compound reacted with *trans*-**1** to produce the C–C coupling compounds coupled at C2 and C3 carbon atoms, rather than C1 carbon atom. The chemoselectivities of the former are different from the Lewis acid-promoted reaction, indicating the synthetic utility of excited state.



Scheme 2 Mukaiyama aldol addition reaction, hetero Diels Alder reaction, and photochemical PB reaction of Danishefsky diene with carbonyl compounds

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